Amendments to the Claims

This listing of claims will replace all prior versions, and listings, of claims in the application:

LISTING OF CLAIMS

1. *(withdrawn):* A method for making a prognosis of enhanced or reduced recovery from an inflammatory condition in a subject having, or at risk of developing, the inflammatory condition, the method comprising:

determining a genotype defined by one or more polymorphic sites in the plasminogen-activator-inhibitor-1 (PAI-1) gene in the subject, wherein said genotype is predictive or indicative of an enhanced or reduced ability of the subject to recover from the inflammatory condition compared to a subject not having the genotype,

with the proviso that the one or more polymorphic sites is not a single polymorphism solely at nucleotide position 837 of SEQ ID NO:1.

2. *(withdrawn):* The method of claim 1, wherein the one or more polymorphic sites includes position 12580 of SEQ ID NO:1 or a polymorphic site in total linkage disequilibrium thereto.

3. *(withdrawn):* The method of claim 2, wherein the one or more polymorphic sites is selected from the group consisting of positions 5645, 7121, 7437, 8070, 8406, 9463, 9466, 12219, 12580, 13889 and 14440 of SEQ ID NO:1.

4. *(withdrawn):* The method of claim 1, wherein the genotype is defined by a combination of two or more polymorphic sites, the combination being a grouping of the following nucleotides positions of SEQ ID NO:1:

(A) 664 A and 2037 T;

(B) 664 A and 2362 deletion;

(C) 664 A and 2852 A;

(D) 664 A and 5834 A;

(E) 837 deletion and 2037 T;

(F) 837 deletion and 2362 deletion;

(G) 837 deletion and 2852 A;

(H) 837 deletion and 5834 A;

(I) a combination of three of the following polymorphic nucleotides:

(i) one of 5878 G, 7343 G and 13605 A,

(ii) one of 7365 T, 7729 insertion, 7771 A and 12750 A; and

(iii) one of 4588 T, 5404 G, 5686 A, 5984 A, and 11312 A; or

(J) a combination of four of the following polymorphic nucleotides selected as shown below:

(i) one combination of two nucleotides 2846 A/10381 T, 6821 T/10381 T and 9759 G/10381 T

(ii) one of 7365 T, 7729 insertion, 7771 A and 12750 A; and

(iii) one of 4588 T, 5404 G, 5686 A, 5984 A, and 11312 A;

5. *(withdrawn):* The method of claim 1, further comprising comparing the determined genotype with genotypes known to be indicative of, or associated with, a prognosis of recovery from (i) the inflammatory condition with which the subject is affected or (ii) another inflammatory condition.

6. *(withdrawn):* The method of claim 1, further comprising ascertaining a PAI-1 gene sequence of the subject.

7. *(withdrawn):* The method of claim 1, wherein the genotype determination is performed on a nucleic acid sample from the subject.

8. *(withdrawn):* The method of claim 7, further comprising the step of obtaining the nucleic acid sample from the subject.

9. *(withdrawn):* The method of claim 7, wherein the genotype determination employs one or more of the following methods:

(a) restriction fragment length analysis;
(b) sequencing;
(c) hybridization;
(d) oligonucleotide ligation assay;
(e) ligation rolling circle amplification;
(f) 5' nuclease assay;
(g) a polymerase proofreading method;
(h) allele specific PCR; and
(i) reading sequence data.

10. *(withdrawn):* The method of claim 1, wherein the genotype of the subject is predictive or indicative of a decreased likelihood of recovery from the inflammatory condition.11. *(withdrawn):* The method of claim 10, wherein the subject is critically ill and the prognosis is one of severe cardiovascular or respiratory dysfunction .

12. *(withdrawn):* The method of claim 10, wherein the genotype is selected from single nucleotide polymorphic sites and combined polymorphic sites at the following nucleotide positions of SEQ ID NO:1:

(A) 5645 T;
(B) 7121 G;
(C) 7437 T;
(D) 8070 A;
(E) 8406 C;
(F) 9463 G;
(G) 9466 T;
(H) 12219 C;
(I) 12580 G;

(J) 13889 C;
(K) 14440 A;
(L) 664 A and 2037 T;
(M) 664 A and 2362 deletion;
(N) 664 A and 2852 A;
(O) 664 A and 5834 A;
(P) 837 deletion and 2037 T;
(Q) 837 deletion and 2362 deletion;
(R) 837 deletion and 2852 A; and
(S) 837 deletion and 5834 A.

13. *(withdrawn):* The method of claim 1, wherein the genotype of the subject is predicative or indicative of an increased likelihood of recovery from the inflammatory condition.

14. *(withdrawn):* The method of claim 13, wherein the subject is critically ill and the prognosis is one of less severe cardiovascular or respiratory dysfunction.

15. *(withdrawn):* The method of claim 13, wherein the genotype is selected from the single polymorphic sites and combined polymorphic site sat the following nucleotide positions of SEQ ID NO:1:

(A) 5645 C;
(B) 7121 A;
(C) 7437 C;
(D) 8070 G;
(E) 8406 T;
(F) 9463 A;
(G) 9466 C;
(H) 12219 T;
(I) 12580 T;
(J) 13889 T;
(K) 14440 G;
(L) a combination of three of the following polymorphic nucleotides:
  (i) one of 5878 G, 7343 G and 13605 A,
  (ii) one of 7365 T, 7729 insertion, 7771 A and 12750 A; and
  (iii) one of 4588 T, 5404 G, 5686 A, 5984 A, and 11312 A; **or**
(M) a combination of three of the following polymorphic nucleotides or pairs of polymorphic nucleotides:
  (i) one of 2846 A/10381 T, 6821 T/10381 T and 9759 G
  (ii) one of 7365 T, 7729 insertion, 7771 A and 12750 A; and
  (iii) one of 4588 T, 5404 G, 5686 A, 5984 A, and 11312 A;

16. *(withdrawn):* The method of claim 1, wherein the inflammatory condition is one that is due to, or associated with,: sepsis, septicemia, fever, a bacterial viral, fungal or parasitic infection, a medical or surgical condition associated with increased risk of infection or sepsis, pneumonia, systemic inflammatory response syndrome (SIRS), Acute Respiratory Distress Syndrome (ARDS), acute lung injury, pancreatitis, peritonitis, abdominal abscess, trauma, surgery, chronic inflammatory disease, ischemia, ischemia-reperfusion injury of an organ or tissue, tissue damage due to (i) disease, (ii) chemotherapy (iii) radiotherapy, or a reactionto an ingested, inhaled, infused, injected, or delivered substance, glomerulonephritis, kidney failure and dialysis, immunosuppressive therapy, endocarditis, cystic fibrosis, diabetes mellitus, chronic renal failure, bronchiectasis, chronic obstructive pulmonary disease (COPD), chronic bronchitis, emphysema, asthma, febrile neutropenia, meningitis, septic arthritis, necrotizing fasciitis, splenectomy, other post-pump syndrome, cardiac stun syndrome, myocardial infarction, stroke, congestive heart failure, hepatitis, cirrhosis, epiglotittis, gas gangrene, toxic shock syndrome, mycobacterial tuberculosis, hemolytic uremic syndrome/thrombotic thrombocytopenic purpura, pelvic inflammatory disease, encephalitis, autoimmunity including rheumatoid arthritis, osteoarthritis, systemic lupus erythematosus, inflammatory bowel disease, idiopathic pulmonary fibrosis, sarcoidosis, hypersensitivity pneumonitis, systemic vasculitis, Wegener's granulomatosis; an organ or tissue transplant and/or transplant rejection, graft-versus-host disease, sickle cell anemia, nephrotic syndrome, or toxicity caused by a therapy with a monoclonal antibody or cytokine.

17. *(withdrawn):* The method of claim 16, wherein the inflammatory condition is SIRS .

18. *(withdrawn):* A method of identifying a polymorphism in a PAI-1 gene sequence that correlates with or is associated with a prognosis of recovery from an inflammatory condition in a subject, the method comprising:

(a) obtaining PAI-1 gene sequence information from a plurality subjects ;

(b) based on the sequence information of (a), identifying at least one site of polymorphism in the PAI-1 gene;

(c) determining genotypes defined by said at least one polymorphism for individual subjects ;

(d) determining recovery ability of individual subjects from the inflammatory condition; and

(e) correlating the genotypes determined in step (c) with the subjects' recovery abilities determined in step (d), thereby identifying said polymorphism in said PAI-1 gene.

19. *(withdrawn):* The method of claim 18 wherein the inflammatory condition is one that is due to, or associated with, : sepsis, septicemia, fever, a bacterial viral, fungal or parasitic infection, a medical or surgical condition associated with increased risk of infection or sepsis, pneumonia, SIRS, ARDS, acute lung injury, pancreatitis, peritonitis, abdominal abscess, trauma, surgery, chronic inflammatory disease, ischemia, ischemia-reperfusion injury of an organ or tissue, tissue damage due to (i) disease, (ii) chemotherapy (iii) radiotherapy, or a reactionto an ingested, inhaled, infused, injected, or delivered substance, glomerulonephritis, kidney failure and dialysis, immunosuppressive therapy, endocarditis, cystic fibrosis, diabetes mellitus, chronic renal failure, bronchiectasis, COPD, chronic bronchitis, emphysema, asthma, febrile neutropenia, meningitis, septic arthritis, necrotizing fasciitis, splenectomy, other post-pump syndrome, cardiac stun syndrome, myocardial infarction, stroke, congestive heart failure, hepatitis, cirrhosis, epiglotittis, gas gangrene, toxic shock syndrome, mycobacterial tuberculosis, hemolytic uremic syndrome/thrombotic thrombocytopenic purpura, pelvic inflammatory disease, encephalitis, autoimmunity including rheumatoid arthritis, osteoarthritis, systemic lupus erythematosus, inflammatory bowel disease, idiopathic pulmonary fibrosis, sarcoidosis,

hypersensitivity pneumonitis, systemic vasculitis, Wegener's granulomatosis; an organ or tissue transplant and/or transplant rejection, graft-versus-host disease, sickle cell anemia, nephrotic syndrome, or toxicity caused by a therapy with a monoclonal antibody or a cytokine.

20. *(previously presented):* A kit useful for determining a genotype of a subject or subjects at a defined polymorphic nucleotide position in a PAI-1 gene sequence from the subject or subjects which genotype is associated with a prognosis of the subject's ability to recover from an inflammatory condition, the kit comprising, in a package:

(a) a restriction enzyme with specificity that distinguishes alternate nucleotides at the polymorphic site or sites; or

(b) a labeled oligonucleotide having sufficient complementarity to a sequence that is contiguous with or near the polymorphic site such that the oligonucleotide hybridizes in a distinguishable manner to a sequence that comprises alternate nucleotide or nucleotides at the polymorphic site or sites,

with the proviso that the polymorphism is not solely at position 837 of SEQ ID NO:1.

21. *(currently amended):* The kit of claim 20, wherein the polymorphic site is at one or more of nucleotide positions [[5645]], 7121, 7437, 8070, 8406, 9463, 9466, 12219, 12580, 13889 and 14440 of SEQ ID NO:1.

22. *(previously presented):* The kit of claim 21, where the polymorphic site is nucleotide position 12580 of SEQ ID NO:1.

23. *(currently amended):* The kit of claim 21[20] comprising said restriction enzyme and an oligonucleotide primer or a set of oligonucleotides suitable to amplify a region flanking the polymorphic site.

24. *(previously presented):* The kit of claim 23, further comprising a polymerization agent that promotes or permits nucleotide polymerization.

25. *(currently amended):* The kit of claim 21[[20]], further comprising instructions for using the kit to determine genotype.

26. *(withdrawn):* A method for identifying subjects as being suitable for a trial that tests efficacy of a candidate drug known to be, or suspected of being, useful for the treatment of an inflammatory disease or condition, the method comprising

(a) determining a genotype defined by one or more polymorphic sites in the PAI-1 gene for each subject, wherein said genotype is indicative of the subject's recovery ability from the inflammatory condition; and

(b) sorting subjects into a suitable or unsuitable group for said trial based on the subjects' genotype,

with the proviso that the polymorphic site is not solely position 837 of SEQ ID NO:1.

27. *(withdrawn):* A method for testing a candidate drug for its efficacy in the treatment of an inflammatory disease or condition wherein said disease or condition is associated with a genotype defined by a polymorphism in a PAI-1 gene, comprising:

(a) identifying subjects that are suitable for a trial that tests said candidate drug in accordance with claim 26; and

(b) administering said candidate drug to each of said subjects, and comparing the subjects' responses to said candidate drug in comparison with the subjects' genotype,

thereby testing said candidate drug.

28. *(withdrawn):* The method of claim 27, wherein a subject's response to said candidate drug is measured as the ability to recover from the inflammatory condition.